REMARKS

Claims 1-22 are pending in this application. Claims 9, 10, 12 and 13 have been cancelled. Claims 1-8 and 11 have been amended. New claims 14-22 have been added.

As in the parent application no. 09/700,187, the specification has been amended to identify all sequences by a sequence identifier. All primers have sequence identification numbers and accordingly, the specification has been amended as shown above to insert sequence identification numbers that correspond to the sequences in the sequence listing filed in computer format in application no. 09/700,187 and attached hereto in paper format. The applicant submits that the presently amended specification fully complies with 37 CFR 1.821 - 1.825.

In accordance with 37 CFR 1.821(c), a "Sequence Listing" is submitted herewith, and it is respectfully requested that the Listing be entered into the application. The Sequence Listing does not include new matter.

Attached is a copy of a Letter Requesting Transfer Of Previously Filed Sequence Listing Pursuant To 37 CFR 1.821(e) which was separately filed in the Patent and Trademark Office in this application on February 10, 2005. The previously filed sequence listing was in computer readable form and was filed in parent application no. 09/700,187.

In accordance with 37 CFR 1.821(f), it is submitted that the contents of the attached paper copy and the previously filed computer readable copy of the Sequence Listing are the same.

In view of the above, it is respectfully submitted that the above-identified application complies with the Requirements for Patent Applications Containing Nucleotide Sequence and/or Amino Acid Sequence Disclosures.

With respect to the rejections in the Office Action dated May 27, 2003 in the parent application no. 09/700,187, the applicants provide the following remarks supporting allowance of the presently pending claims.

In response to the Examiner's concerns under 35 USC 112, second paragraph regarding a constitutive promoter, claim 3 has been amended to change the term "a constitutive promoter" to "the constitutive promoter".

The term "cis-element" is well known. Two definitions apply, "a DNA sequence contiguous to transcribed region that plays a role in regulating the transcription of the gene", or "Control sequences such as the 0 gene, which are only active on the same DNA molecule as the genes they control, are called cis-acting elements" (Please refer to the two references attached hereto as "Technical References").

With respect to the claim rejections under 35 USC 102, the Office Action stated that "Strasberg et. al., Okubo et al, and Adams, et al, recite SEQ ID No:1 and thus expression of a polynucleotide sequence placed downstream of SEQ ID NO:1 and a promoter operably linked to said polynucleotide sequence would inherently be repressed in the presence of light. Accordingly, Strasberg et. al., Okubo et al, and Adams anticipate the claimed invention."

The applicants respectfully disagree. Please note that the presently claimed invention includes an <u>isolated</u> DNA fragment. Strasberg et. al.,

Okubo et al, and Adams do not disclose any isolated DNA fragment containing the sequence of SEQ ID NO:1, nor the possibility that the sequence of SEQ ID NO:1 when isolated can be used as a cis-element to repress expression of a gene placed downstream of SEQ ID NO:1 under the presence of light. Moreover, the DNA sequences disclosed in Strasberg et. al., Okubo et al, and Adams (Accession AA579315, Accession D25785 and Accession AQ009485) are ESTs, i.e., derived from the transcribed mRNAs. Accordingly, the applicants submit that a person of ordinary skill in the are would find that the sequences of these references do not act as a cis-element in their natural position.

With respect to the claim rejections under 35 USC 112, first paragraph (written description), concerning the term "nucleotide sequence obtained by deletion, substitution and/or addition of one or more bases in SEQ ID NO:2, other than SEQ ID NO:1", the Office Action stated that "Applicant has not given a representative number of additions, substitutions and/or deletions which have the desired function".

In response the claims have been amended as shown above to delete the term "additions, substitutions". As for "deletions", the applicants respectfully submit that the present specification contains sufficient support.

With respect to the claim rejections under 35 USC 112, first paragraph (new matter), the applicants submit that "a promoter operatively linked to said gene" does not constitute new matter. From the context of the presently described invention as set forth in the

specification, it would be clear to those skilled in the art that the promoter and the peptide-coding sequence are linked operatively. For example, please refer to Example 9 of the present application, wherein the 12-bp core sequence, the promoter of CaMV 35S90 are linked operatively.

Entry of this amendment and favorable consideration of this application are respectfully requested.

Respectfully submitted,

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APPENDIX

COPY OF LETTER REQUESTING TRANSFER OF PREVIOUSLY FILED SEQUENCE LISTING IN PARENT US APPLICATION NO. 09/700,187

COPIES OF TECHNICAL REFERENCES

「"definition of cis-element"」の検索結果 12件 中 1〜9件表示

msword Eukaryotic Gene Regulation
... See Overhead. Cis and Trans Elements. Definition of Cis Element · A DNA sequence contiguous to transcribed region that plays a role in regulating the transcription of the gene. Types of Cis Elements. Two Factors differentiate cis factors · location and effect on regulation. ...
http://faculty.buffalostate.edu/wadswogj/courses/303/Eukaryotic%2520Gene%2520Regulation.doc - キャッシュ - 関連ページ

JBC -- Abstracts: Devajyothi et al. 268 (25): 18794
J. Biol. Chem., Vol. 268, Issue 25, 18794-18800, 09, 1993. Inhibition of interferon-gamma-induced major histocompatibility complex class II gene transcription by interferon-beta and type beta 1 transforming growth factor in human astrocytoma cells. Definition of cis-element. ...
http://www.jbc.org/cgi/content/abstract/268/25/18794 - 関連ページ

JBC -- Search Result
... interferon-gamma-induced major histocompatibility complex class II gene transcription by interferon-beta and type beta 1 transforming growth factor in human astrocytoma cells. Definition of cis-element J. Biol. Chem., Sep 1993; 268: 18794 - 18800 . ...
http://www.jbc.org/cgi/search%3Fqbe%3Djbc%3BM110538200%26journalcode%3Djbc%26minscore%3D5000 - 関連ページ
[このサイト内の検索結果]

CWRU Physiology and Biophysics
... Devajyothi, C., Kalvakolanu, I., Babcock, GT, Vasavada, HA, PH Howe, and Ransohoff, RM Inhibition of interferon g induced major histocompatibility complex class II gene transcription by interferon b and transforming growth factor b1 in human astrocytoma cells: definition of cis-element. J. Biol. ...
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AUTOIMMUNE ASPECTS OF CYTOKINES AND ANTI-CYTOKINE THERAPIES
... 108. Devajyothi C, Kalvakolanu I, Babcock GT, Vasavada HA, Howe PH, Ransohoff RM: Inhibition of interferon-gamma-induced
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pdf FIBROMYALGIA: COULD IT BE IN YOUR MIND
Page 1. from http://www.rheuma21st.com AUTOIMMUNE ASPECTS OF CYTOKINES AND ANTI-CYTOKINE
THERAPIES Reported by Irit Krause, Yehuda Shoenfeld Nephrology and Dialysis Unit, Schneider' s Children Medical Center of Israel, Petah-Tiqva, Israel, Center ...
http://www.rheuma21st.com/downloads/cutting_edge_cyto_therapy_shoenfeld.pdf - キャッシュ - 関連ページ

pdf Astrocytic Factors Deactivate Antigen Presenting Cells that Invade ...
Page 1. Nils P. Hailer 1 , Frank L. Heppner 2 , Dorit Haas 2 , Robert Nitsch 2 1 University Hospital for Orthopedic Surgery "Friedrichsheim", Marienburgstr. 2, D - 60528 Frankfurt am Main, Federal Republic of Germany 2 Department of Cell- and ...
http://brainpath.medsch.ucla.edu/pdfs/0803pdf/hailer.pdf - 関連ページ

The JI -- Han et al. 163 (3): 1435
... [Abstract/Free Full Text]; Devajyothi, C., I. Kalvakolanu, GT Babcock, HA Vasavada, PH Howe, RM Ransohoff. 1993. Inhibition of interferon- -induced gene transcription by interferon and type 1 transforming growth factor in human astrocytoma cells: definition of cis element. J. Biol. Chem. 268:18794. ...
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... 1993. Inhibition of interferon- -induced major histocompatibility complex class II gene transcription by interferon-ß and type ß1 transforming growth factor in human astrocytoma cells: definition of cis-element.
J. Biol. Chem. 268:18794. [Abstract/Free Full Text]; Fast, DJ, RC Lynch, RW Leu. 1993. ...

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expected, there was no β-galactosidase activity because the Hfr donors lacked inducer and the F^- recipients were unable to produce active enzyme (only DNA passes through the cytoplasmic bridge connecting mating bacteria). About 1 h after conjugation began, however, when the I^+Z^+ genes had just entered the F^- cells, β-galactosidase synthesis began and only ceased after about another hour. The explanation for these observations is that the donated Z^+ gene, upon entering the cytoplasm of the I^- cell, directs the synthesis of β-galactosidase in a constitutive manner. Only after the donated I^+ gene has had sufficient time to be expressed is it able to repress β-galactosidase synthesis. *The I^+ gene must therefore give rise to a diffusible product, the lac repressor, which inhibits the synthesis of β-galactosidase (and the other lac proteins).* Inducers such as IPTG temporarily inactivate *lac* repressor, whereas I^- cells constitutively synthesize *lac* enzymes because they lack a functional repressor. *Lac* repressor, as we shall see in Section 29-3B, is a protein.

B. Messenger RNA

The nature of the *lac* repressor's target molecule was deduced in 1961 through a penetrating genetic analysis by Jacob and Monod. A second type of constitutive mutation in the lactose system, designated O^c (for operator constitutive), which complementation analysis has indicated to be independent of the *I* gene, maps between the *I* and *Z* genes (Fig. 29-3). In the partially diploid *F'* strain $O^cZ^-/F\ O^+Z^+$, β-galactosidase activity is inducible by IPTG whereas the strain $O^cZ^+/F\ O^+Z^-$ constitutively synthesizes this enzyme (in F' bacteria, the F factor plasmid contains a segment of the bacterial chromosome, in this case a portion of the *lac* operon; Section 27-1D). *An O^+ gene can therefore only control the expression of a Z gene on the same chromosome.* The same is true with the Y^+ and A^+ genes.

Jacob and Monod's observations led them to conclude the proteins are synthesized in a two-stage process:

1. The structural genes on DNA are transcribed onto complementary strands of messenger RNA (mRNA).
2. The mRNAs transiently associate with ribosomes, which they direct in polypeptide synthesis.

This hypothesis explains the behavior of the *lac* system *(Fig. 29-5). In the absence of inducer, the lac repressor specifically binds to the O gene (the operator) so as to physically block the enzymatic transcription of mRNA. Upon binding inducer, the repressor dissociates from the operator, thereby permitting the transcription and subsequent translation of the lac enzymes.* The operator–repressor–inducer system thereby acts as a molecular switch so that the *lac* operator can only control the expression of *lac* enzymes on the same chromosome. The O^c mutants constitutively synthesize *lac* enzymes because they are unable to bind repressor. The coordinate (simultaneous) expression of all three *lac* enzymes under the control of a single operator site arises, as Jacob and Monod theorized, from the transcription of the *lac* operon as a single polycistronic mRNA which directs the ribosomal synthesis of each of these proteins. This transcriptional control mechanism is further discussed in Section 29-3. [DNA sequences, which are on the same DNA molecule, are said to be in cis (Latin: on this side), whereas those on different DNA molecules are said to be in trans (Latin: across). Control sequences such as the *O* gene, which are only active on the same DNA molecule as the genes they control, are called **cis-acting elements**. Those such as *lacI*, which specify the synthesis of diffusible products and can therefore be located on a different DNA molecule from the genes they control, are said to direct the synthesis of **trans-acting factors**.]

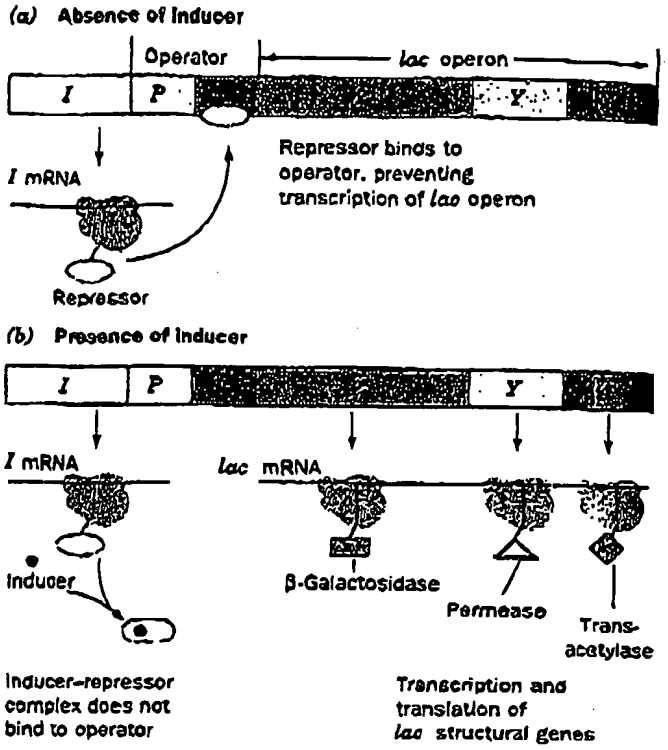

FIGURE 29-5. The expression of the *lac* operon. (*a*) In the absence of inducer, the repressor, the product of the *I* gene, binds to the operator, thereby preventing transcription of the *lac* operon. (*b*) Upon binding inducer, the repressor dissociates from the operator, which permits the transcription and subsequent translation of the *lac* structural genes to proceed.

mRNAs Have Their Predicted Properties

The kinetics of enzyme induction, as indicated, for example, in Figs. 29-2 and 29-4, requires that the postulated mRNA be both rapidly synthesized and rapidly degraded. An RNA with such quick turnover had, in fact, been observed in T2-infected *E. coli*. Moreover, the base composition of this RNA fraction resembles that of the viral DNA